DOCKET NO.: NIHC-6039 Application No.: 10/594,075

Advisory Action Dated: December 5, 2011

### REMARKS

These remarks accompany a Request for Continued Examination (RCE), a request for a three month extension of time, a Rule 132 Declaration of Dr. Joseph J. Barchi, Jr., Ph.D (Exhibit A), and the *curiculum vitae* (CV) of Dr. Joseph J. Barchi, Jr., Ph.D (Exhibit B).

Claims 95, 98, 150 and 155 have been finally rejected. Claims 96-97 were previously cancelled and claims 99-149 and 151-154 were previously withdrawn.

Applicants thank the examiner for entering the amendments listed in their amendment and response to the previous office action (final rejection), as indicated in the Advisory Action mailed 5 December 2011.

The Advisory Action also indicates that the arguments and amendments filed 11 August 2011 have been fully considered and are persuasive to overcome the rejections under 35 USC 112, paragraph 2.

## I. The Rejections Under 35 U.S.C. 103 Should be Withdrawn

Various claims stand rejected under 35 U.S.C. 103(a) as allegedly unpatentable over various prior art references. But because the cited art does not contemplate applicants' claimed quantum dots, these rejections should be reconsidered and withdrawn.

# A. Legal Standard

To establish a *prima facie* case of obviousness, there must be a clearly articulated reason or rationale, either in the prior art itself or in the knowledge generally available to one of ordinary skill in the art, why the claimed invention is obvious in light of a reference or combined reference teachings. MPEP §§ 2143, 2143.01; *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739-43 (2007). There must also be a reasonable expectation of success. MPEP § 2143.02. Further, the prior art combination must address all of the elements of the claim at issue. MPEP § 2143.03. The rationale to make the claimed combination and the reasonable expectation of success must be found in the prior art and not be based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991).

### B. Discussion

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<u>First</u>, claim 95 is patentable over the Zheng reference in view of the Lin reference and the Bawendi patent. No combination of these references teaches a quantum dot capable of luminescing, comprising:

a nanocrystalline core exhibiting quantum confinement and having a band gap;

a luminescence promoter linked to the surface of the nanocrystalline core, the luminescence promoter comprising a mercapto triethylene glycol group that does not have an associated charge in solution.

More specifically, Zheng fails to contemplate all of these claim elements and in fact teaches away from applicants' approach. As explained in the attached declaration (Exhibit A) of Dr. Joseph J. Barchi, Jr., Ph.D., one of ordinary skill in the art would not understand how the Lin and Bawendi references would provide any motivation to modify the disclosure of the Zheng reference to arrive at the invention claimed in the subject application (Exhibit A at ¶ 5). Specifically, one of ordinary skill in the art would understand the Zheng reference to be directed to solving problems associated with non-specific binding of metallic nanomaterials with biological molecules via electrostatic interactions. Such non-specific binding of metallic nanomaterials with biological molecules via electrostatic interactions is quite different from the claimed quantum dots (Exhibit A at ¶ 6).

The Zheng reference also describes generally that it is recognized that the surfaces of many metallic nanoparticles, such as Au, Ag, Pt and Cu are charged, which cause nonspecific binding with biological molecules via electrostatic interactions (Zheng, p. 7790, left col., first par., II. 7-10) (Exhibit A at ¶ 8). As explained further in this paragraph of Zheng, nonspecific binding between nanoparticles and biomolecules is a fundamental issue that is not well addressed in the published literature (Exhibit A at ¶ 9). Zheng solves the problem of the electrostatic-driven non-specific binding between metallic gold nanoparticles and biological molecules by bonding a uniform monolayer of di-, tri-, and tetra(ethylene glycol) to the surfaces of the gold nanoparticles (Exhibit A at ¶ 10).

Dr. Barchi explains that it is known that noble metal nanoparticles, like gold and silver, are conductors and so they <u>do not have a band gap</u>. For this reason <u>metallic nanoparticles do</u> not typically luminesce. Instead, these materials are characterized by intense, size-dependent

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surface plasmon absorption in the visible or near-ultraviolet region when the particle size is decreased below the de Broglie wavelength of 20 nm. When electrons are promoted into the conduction band, they become trapped and exhibit a characteristic oscillation known as the surface plasmon band. If the wavelength of incident light corresponds to that of the conduction band electrons, enhanced oscillation of the electron cloud results. This is referred to as the localized surface plasmon resonance (LSPR). The result is a strong absorbance at an energy that is unique for sufficiently small (~5-20 nm) noble metal nanoparticles (Exhibit A at ¶ 11).

As further explained by Dr. Barchi, it is known that the LSPR is sensitive to changes in refractive index that can be incurred by changes in particle size and/or surface functionalization of metallic nanoparticles (Exhibit A at ¶ 12). Accordingly, surface functionalization methods must be very specifically tailored to the type and size of noble metal nanoparticles to ensure that LSPR occurs (Exhibit A at ¶ 13). As a result, the surface functionalization methods that may very well be useful for allowing noble metal nanoparticles to exhibit LSPR would not motivate one of ordinary skill in the art to use the same functionalization startegies on luminescing nanoparticles that exhibit a band gap, such as those claimed in the subject application (Exhibit A at ¶ 14).

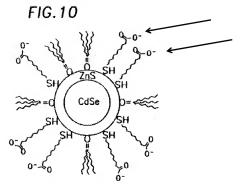
Because the Zheng reference discloses only the problems associated with the charged surfaces of metallic nanoparticles, one of skill in the art would not be motivated to look towards the Zheng reference as a starting point for making quantum dots capable of luminescing and comprising a nanocrystalline core exhibiting quantum confinement and having a band gap as claimed in the subject application (Exhibit A at ¶ 15).

The Lin reference is also directed to metallic gold nanoparticles that are quite unlike the nanoparticles claimed in the subject application. The examiner had indicated (final rejection page 4, second full paragraph), that Lin teaches that besides gold nanoparticles, semiconductor nanoparticle bioconjugates as selective fluorescent biological labels have shown great potential in biological studies and medical applications (Lin, II. 1-13, 1st col, p. 3508). This may be so, generally speaking, but Lin still does not teach any chemical methods or compositions specifically in connection with semiconductor quantum dots having a band gap as claimed in the subject application (Exhibit A at ¶ 16).

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The Bawendi patent discloses functionalizing semiconducting nanoparticles with thiols. However, the particular thiols of Bawendi in Figure 10 (indicated below by arrows) the examiner refers to in the final rejection in the third full paragraph of page 4 are actually charged thiols ending in charged carboxylic acid groups.



The highlighted groups are quite different from the mercapto triethylene glycol group that does not have an associated charge in solution (Exhibit A at ¶ 19). For example, claim 155 is directed to luminescence promoters comprising a plurality of mercapto triethylene glycol groups of the formula.

which formula has a methoxy group on the left end; this is completely different than the charged carboxylic acid groups shown in Bawendi Figure 10 (Exhibit A at  $\P$  20).

<u>Second</u>, claims 96, 150 and 155 are patentable because they depend from non-obvious independent claim 95, as discussed above. Accordingly, the rejections of these claims should be

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reconsidered and withdrawn. E.g., In re Fine, 837 F.2d 1071, 1076 (Fed. Cir. 1988) (claims depending from nonobvious independent claim are themselves nonobvious).

### II. Conclusions

Applicants request the amendments and new claims be added and, accordingly to reconsider and withdraw the rejections. Applicants submit that all rejections concerning the patent application have been addressed and urge the examiner to pass the application to allowance. If there are any remaining issues, the examiner is requested to telephone the undersigned attorney.

Respectfully submitted,

Date: January 9, 2012 /Jeffrey H. Rosedale/

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